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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
NEWS 14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 21	NOV 13	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 22	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 23	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 24	NOV 20	CA/CAplus patent kind codes will be updated
NEWS 25	DEC 01	CAS REGISTRY updated with new ambiguity codes

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
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NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 15:22:26 ON 04 DEC 2006

=> fil medline biosis caplus scisearch embase wpids
COST IN U.S. DOLLARS

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FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 15:22:53 ON 04 DEC 2006

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FILE 'WPIDS' ENTERED AT 15:22:53 ON 04 DEC 2006
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=> enzyme (s) (competitive or ?competitive) (s) inhibi? and nmr
L1 315 ENZYME (S) (COMPETITIVE OR ?COMPETITIVE) (S) INHIBI? AND NMR

=> (library or scree or identif) (s) (ligand or compound) and L1
UNMATCHED RIGHT PARENTHESIS ') '
The number of right parentheses in a query must be equal to the number of left parentheses.

=> (library or scree? or identif?) (s) (ligand or compound) and L1
L2 5 (LIBRARY OR SCREE? OR IDENTIF?) (S) (LIGAND OR COMPOUND) AND L1

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 2 DUP REM L2 (3 DUPLICATES REMOVED)

=> d ibib abs l3 1-2

L3 ANSWER 1 OF 2 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-312892 [30] WPIDS
DOC. NO. CPI: C2003-082045 [30]
TITLE: Novel crystalline complex of human type III 3 alpha-hydroxysteroid dehydrogenase enzyme and NADP, useful for designing and selecting novel class of modulators to the enzyme
DERWENT CLASS: B04; B05; D16
INVENTOR: FLOERSHEIM P; JAHNKE W; OSTERMEIER C; UZUNOV D
PATENT ASSIGNEE: (FLOE-I) FLOERSHEIM P; (JAHN-I) JAHNKE W; (NOVS-C) NOVARTIS AG; (NOVS-C) NOVARTIS PHARMA GMBH; (OSTE-I)

OSTERMEIER C; (UZUN-I) UZUNOV D
COUNTRY COUNT: 88

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003018830	A2	20030306	(200330)*	EN	156[0]	
EP 1421383	A2	20040526	(200435)	EN		
AU 2002333508	A1	20030310	(200452)	EN		
JP 2005500853	W	20050113	(200506)	JA	300	
US 20050202505	A1	20050915	(200561)	EN		
AU 2002333508	A8	20051020	(200615)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003018830	A2	WO 2002-EP9366	20020821
US 20050202505	A1 Provisional	US 2001-314045P	20010822
AU 2002333508	A1	AU 2002-333508	20020821
EP 1421383	A2	EP 2002-796261	20020821
EP 1421383	A2	WO 2002-EP9366	20020821
JP 2005500853	W	WO 2002-EP9366	20020821
US 20050202505	A1	WO 2002-EP9366	20020821
JP 2005500853	W	JP 2003-523677	20020821
US 20050202505	A1	US 2004-486660	20040212
AU 2002333508	A8	AU 2002-333508	20020821

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1421383	A2 Based on	WO 2003018830 A
AU 2002333508	A1 Based on	WO 2003018830 A
JP 2005500853	W Based on	WO 2003018830 A
AU 2002333508	A8 Based on	WO 2003018830 A

PRIORITY APPLN. INFO: US 2001-314045P 20010822
US 2004-486660 20040212
AN 2003-312892 [30] WPIDS
AB WO 2003018830 A2 UPAB: 20060119

NOVELTY - A crystalline complex (I) of a human type III 3alpha-hydroxysteroid dehydrogenase (3a-HSD) enzyme and NADP exhibiting essentially the atomic co-ordinates given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) Producing (I), by growing (I) in 50-200 mM ammonium sulfate or ammonium acetate, 25-200 mM MES, pH 6.0 or 25-200 mM sodium citrate, 20-30% polyethylene glycol (PEG) monomethylether 2000 or 5000 or 20-30% PEG 2000, 4000, 6000 or 8000, 0-10% additives and 0-20 mM dithiotheritol (DTT); and

(2) Identifying (M) an inhibitor of the human type III 3a-HSD enzyme, by designing or selecting computationally a potential inhibitor by using the atomic coordinates of the human type III 3a-HSD enzyme or co-complexes, e.g. as given in the specification, obtaining a potential inhibitor by performing a nuclear magnetic resonance (NMR) screen with the human type III 3a-HSD and candidate compounds, e.g., from a library of compounds, obtaining a potential inhibitor by performing a NMR reporter screen with the human type III 3a-HSD, a first inhibitor candidate to human type III 3a-HSD with a dissociation constant smaller than 2 mM which is either

already known or found by the above mentioned steps, and further a second candidate compound, e.g. from a library of compounds, and/or determining the activity of the potential inhibitor from the above mentioned steps at the human type III 3a-HSD enzyme.

USE - The method is useful for identifying (M) an inhibitor of the human type III 3a-HSD enzyme and producing a crystalline complex (claimed). The structural co-ordinates of (I) are useful for designing and selecting novel class of modulators to human type III 3a-HSD, for revealing the atomic details of the active site or the co-factor binding site of the enzyme and to solve the structure of a different human type III 3a-HSD crystal, or a crystal of a mutant, homolog or co-complex, of human type III 3a-HSD, or for providing potentiators or inhibitors of human type III 3a-HSD.

L3 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 91198133 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2015295
TITLE: The inhibition of rat liver threonine dehydratase by carbamoyl-phosphate. The formation of carbamoylpyridoxal 5'-phosphate.
AUTHOR: Pagani R; Ponticelli F; Terzuoli L; Leoncini R; Marinello E
CORPORATE SOURCE: Institute of Biological Chemistry, University of Siena, Italy.
SOURCE: Biochimica et biophysica acta, (1991 Apr 8) Vol. 1077, No. 2, pp. 233-40.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 7 Jun 1991
Last Updated on STN: 7 Jun 1991
Entered Medline: 23 May 1991

AB The effects exerted by carbamoyl phosphate (CP) and cyanate (KCNO) on rat liver L-threonine deaminase have been studied. The two compounds showed that same effects, inhibiting through a competitive mechanism both the holoenzyme and the dialyzed enzyme; inhibition was more evident for the latter. Ki values, both for L-threonine and pyridoxal 5'-phosphate (PLP), were lower for the apoenzyme and the inhibitors also affected the Km of the apoenzyme for PLP. The effects of CP and KCNO are mainly due to an interference in the association reaction apoenzyme + PLP in equilibrium holoenzyme This was clearly demonstrated by the fact that, when PLP was incubated with CP or KCNO, it failed to enhance the activity of the holoenzyme nor did it reactivate the resolved apoenzyme. Such interference of CP and KCNO in the L-threonine deaminase activity was mainly due to a specific mechanism, the formation of a new derivative of PLP. The reaction of PLP with either CP or KCNO occurred readily, at low concentrations, under physiological conditions. The new compound was identified as 3,4-dihydro-2H-pyrido[3,4-e]1,3-oxazin-2-one derivative by ultraviolet-visible spectra, elemental analysis, infrared, NMR and MS spectra. In this paper we formulate the hypothesis that this compound is involved in the regulation of the CP and PLP intracellular content and in the control of PLP dependent enzymes.

=> (library or scree? or identif?) (s) (ligand or compound)
L4 77053 (LIBRARY OR SCREE? OR IDENTIF?) (S) (LIGAND OR COMPOUND)

=> d his

(FILE 'HOME' ENTERED AT 15:22:26 ON 04 DEC 2006)

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT 15:22:53 ON 04 DEC 2006

L1 315 ENZYME (S) (COMPETITIVE OR ?COMPETITIVE) (S) INHIBI? AND NMR
L2 5 (LIBRARY OR SCREE? OR IDENTIF?) (S) (LIGAND OR COMPOUND) AND L1
L3 2 DUP REM L2 (3 DUPLICATES REMOVED)
L4 77053 (LIBRARY OR SCREE? OR IDENTIF?) (S) (LIGAND OR COMPOUND)

=> py>1999 and l1
L5 101 PY>1999 AND L1

=> l1 not l5
L6 214 L1 NOT L5

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 94 DUP REM L6 (120 DUPLICATES REMOVED)

=> t ti l7 1-50

L7 ANSWER 1 OF 94 MEDLINE on STN DUPLICATE 1
TI Beta-lactones as a new class of cysteine proteinase inhibitors: inhibition of hepatitis A virus 3C proteinase by N-Cbz-serine beta-lactone.

L7 ANSWER 2 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Enzymatic activity and beta-galactomannan binding property of beta-mannosidase from Trichoderm reesei.

L7 ANSWER 3 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Polyhydroxylated pyrrolidine and pyrrolizidine alkaloids from Hyacinthoides non-scripta and Scilla campanulata.

L7 ANSWER 4 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Indoleamine analogs as probes of the substrate selectivity and catalytic mechanism of serotonin N-acetyltransferase.

L7 ANSWER 5 OF 94 MEDLINE on STN DUPLICATE 2
TI Catalytic mechanism of Kdo8P synthase: transient kinetic studies and evaluation of a putative reaction intermediate.

L7 ANSWER 6 OF 94 MEDLINE on STN DUPLICATE 3
TI Potent peptide inhibitors of human hepatitis C virus NS3 protease are obtained by optimizing the cleavage products.

L7 ANSWER 7 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Chemo-enzymatic synthesis of galactosylmaltooligosaccharidonolactone as a substrate analogue inhibitor for mammalian alpha-amylase

L7 ANSWER 8 OF 94 MEDLINE on STN DUPLICATE 4
TI Insight into naphthoquinone metabolism: beta-glucosidase-catalysed hydrolysis of hydrojuglone beta-D-glucopyranoside.

L7 ANSWER 9 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Synthesis and biological evaluation of ureido and thioureido derivatives of 2-amino-2-deoxy-D-glucose and related aminoalcohols as N-acetyl-beta-D-hexosaminidase inhibitors.

L7 ANSWER 10 OF 94 MEDLINE on STN DUPLICATE 5
TI Expression and secondary structure determination by NMR methods of the major house dust mite allergen Der p 2.

L7 ANSWER 11 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Mammalian alkaline phosphatases are allosteric enzymes

L7 ANSWER 12 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Inhibition of Ascorbate Oxidase by Phenolic Compounds. Enzymic and Spectroscopic Studies

L7 ANSWER 13 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Quantitation of metabolic and radiobiological effects of 6-aminonicotinamide in RIF-1 tumor cells in vitro

L7 ANSWER 14 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Looking for residues involved in the muscle acylphosphatase catalytic mechanism and structural stabilization: Role of Asn41, Thr42, and Thr46

L7 ANSWER 15 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
TI Chymotrypsin inhibitory conformation induced by amino acid side chain-side chain intramolecular CH/π interaction

L7 ANSWER 16 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of S-(2-Nitrophenyl)-L-cysteine S-oxide.

L7 ANSWER 17 OF 94 MEDLINE on STN DUPLICATE 7
TI Calystegine B4, a novel trehalase inhibitor from Scopolia japonica.

L7 ANSWER 18 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 8
TI Lipoxygenase-1 inhibition with a series of half-product analogs.

L7 ANSWER 19 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI MECHANISM FOR THE COUPLING OF ATP HYDROLYSIS TO THE CONVERSION OF 5-FORMYLTETRAHYDROFOLATE TO 5,10-METHENYLTETRAHYDROFOLATE

L7 ANSWER 20 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Regulation of mitochondrial and cytosolic malic enzymes from cultured rat brain astrocytes

L7 ANSWER 21 OF 94 MEDLINE on STN DUPLICATE 9
TI Role of methionine in the active site of alpha-galactosidase from Trichoderma reesei.

L7 ANSWER 22 OF 94 MEDLINE on STN DUPLICATE 10
TI Visoltricin, a novel biologically active compound produced by Fusarium tricinctum.

L7 ANSWER 23 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI PREPARATIONS OF PSI-PEPTIDE BOND AND PEPTIDE-ALDEHYDE INHIBITORS OF ATRIAL GRANULE SERINE PROTEINASE, A CANDIDATE PROCESSING ENZYME OF PROATRIAL NATRIURETIC FACTOR

L7 ANSWER 24 OF 94 MEDLINE on STN DUPLICATE 11
TI Vanadium-diascorbates are strong candidates for endogenous ouabain-like factors in human urine: effects on Na-K-ATPase enzyme kinetics.

L7 ANSWER 25 OF 94 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

TI Di:terpenyl peptide cysteinyl protein proteolysis inhibitors - inhibit

proteolysis of ras-protein and neoplastic cell growth

L7 ANSWER 26 OF 94 MEDLINE on STN DUPLICATE 12
TI A stable isotope-aided NMR study of the active site of an endoglucanase from a strain of Bacillus.

L7 ANSWER 27 OF 94 MEDLINE on STN DUPLICATE 13
TI Isotopic exchange plus substrate and inhibition kinetics of D-xylose isomerase do not support a proton-transfer mechanism.

L7 ANSWER 28 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Spectroscopic properties of the photoproducts of pyridoxal-5'-P irradiation: Catalytic site recognition of ribonuclease A

L7 ANSWER 29 OF 94 MEDLINE on STN DUPLICATE 14
TI Arginine-23 is involved in the catalytic site of muscle acylphosphatase.

L7 ANSWER 30 OF 94 MEDLINE on STN DUPLICATE 15
TI A trisaccharide acceptor analog for N-acetylglucosaminyltransferase V which binds to the enzyme but sterically precludes the transfer reaction.

L7 ANSWER 31 OF 94 MEDLINE on STN DUPLICATE 16
TI Phosphoglucose isomerase: a ketol isomerase with aldol C2-epimerase activity.

L7 ANSWER 32 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI MG2+ AFFECTS THE BINDING OF ADP BUT NOT ATP TO 3-PHOSPHOGLYCERATE KINASE - CORRELATION BETWEEN EQUILIBRIUM DIALYSIS BINDING AND ENZYME-KINETIC DATA

L7 ANSWER 33 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Specific inhibition of chymotrypsin by water-soluble dipeptides

L7 ANSWER 34 OF 94 MEDLINE on STN DUPLICATE 17
TI Conformational changes in phospholipase A2 upon binding to micellar interfaces in the absence and presence of competitive inhibitors. A 1H and 15N NMR study.

L7 ANSWER 35 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI INTERACTION OF RABBIT MUSCLE ALDOLASE AT HIGH IONIC STRENGTHS WITH VANADATE AND OTHER OXOANIONS.

L7 ANSWER 36 OF 94 MEDLINE on STN DUPLICATE 18
TI Phospholipase A2 engineering. Structural and functional roles of highly conserved active site residues tyrosine-52 and tyrosine-73.

L7 ANSWER 37 OF 94 MEDLINE on STN DUPLICATE 19
TI Mapping the substrate-binding site of a human class mu glutathione transferase using nuclear magnetic resonance spectroscopy.

L7 ANSWER 38 OF 94 MEDLINE on STN DUPLICATE 20
TI Studies on ribonucleoside-diphosphate reductase from Escherichia coli. The product dCDP is a competitive inhibitor and functions as a spectroscopic probe for the substrate binding site; demonstration by enzyme kinetics and 1H NMR.

L7 ANSWER 39 OF 94 MEDLINE on STN DUPLICATE 21
TI Mechanistic studies on Azospirillum brasilense glutamate synthase.

L7 ANSWER 40 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Identifying the recognition unit for G protein methylation

L7 ANSWER 41 OF 94 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI INVESTIGATION OF AN OCTAPEPTIDE INHIBITOR OF ESCHERICHIA-COLI RIBONUCLEOTIDE REDUCTASE BY TRANSFERRED NUCLEAR OVERHAUSER EFFECT SPECTROSCOPY

L7 ANSWER 42 OF 94 MEDLINE on STN DUPLICATE 22
TI Conformation of an enzyme-bound substrate of staphylococcal nuclease as determined by NMR.

L7 ANSWER 43 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 23
TI SYNTHESIS OF EPIMERIC 6 7 BISTRIFLUOROMETHYL-8-RIBITYLLUMAZINE HYDRATES STEREOSELECTIVE INTERACTION WITH THE LIGHT RIBOFLAVIN SYNTHASE OF BACILLUS-SUBTILIS.

L7 ANSWER 44 OF 94 MEDLINE on STN DUPLICATE 24
TI Proton and tritium NMR relaxation studies of peptide inhibitor binding to bacterial collagenase: conformation and dynamics.

L7 ANSWER 45 OF 94 MEDLINE on STN DUPLICATE 25
TI The inhibition of rat liver threonine dehydratase by carbamoyl-phosphate. The formation of carbamoylpyridoxal 5'-phosphate.

L7 ANSWER 46 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Dehydroquinate synthase: the use of substrate analogs to probe the late steps of the catalyzed reaction

L7 ANSWER 47 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 26
TI SULFOXIMINE AND SULFODIIMINE TRANSITION-STATE ANALOGUE INHIBITORS FOR CARBOXYPEPTIDASE A.

L7 ANSWER 48 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Carbonyl sulfide: an alternate substrate for but not an activator of ribulose-1,5-bisphosphate carboxylase

L7 ANSWER 49 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Characterization of the inhibitor complexes of cobalt carboxypeptidase A by electron paramagnetic resonance spectroscopy

L7 ANSWER 50 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Kinetic and magnetic resonance studies of the glutamate-43 to serine mutant of staphylococcal nuclease

=> t ti l7 51-94

L7 ANSWER 51 OF 94 MEDLINE on STN DUPLICATE 27
TI Kinetic and ultraviolet spectroscopic studies of active-site mutants of delta 5-3-ketosteroid isomerase.

L7 ANSWER 52 OF 94 MEDLINE on STN DUPLICATE 28
TI Methotrexate 5-aminoallyl-2'-deoxyuridine 5'-monophosphate: a potential bifunctional inhibitor of thymidylate synthase.

L7 ANSWER 53 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI NMR studies of enzyme inhibition

L7 ANSWER 54 OF 94 MEDLINE on STN DUPLICATE 29
TI Lysophosphatidylcholines containing polyunsaturated fatty acids were found

as Na+, K+-ATPase inhibitors in acutely volume-expanded hog.

L7 ANSWER 55 OF 94 MEDLINE on STN DUPLICATE 30
TI Inhibition of adenylosuccinate lyase by L-alanosyl-5-aminoimidazole-4-carboxylic acid ribonucleotide (alanosyl-AICOR).

L7 ANSWER 56 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Dextran-linked 7-deazaguanine - a polymer-bound inhibitor of xanthine oxidase

L7 ANSWER 57 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 31
TI NMR STUDIES ON THE SPATIAL RELATIONSHIP OF AROMATIC DONOR MOLECULES TO THE HEME IRON OF HORSERADISH PEROXIDASE.

L7 ANSWER 58 OF 94 MEDLINE on STN DUPLICATE 32
TI Inhibition of RNA-directed DNA polymerase from avian myeloblastosis virus by a 5-benzyl-6-aminouracil.

L7 ANSWER 59 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Fish egg polysialoglycoproteins: circular dichroism and proton nuclear magnetic resonance studies of novel oligosaccharide units containing one sialidase-resistant N-glycolylneuraminic acid residue in each molecule

L7 ANSWER 60 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 33
TI SPIN-LABEL STUDIES ON THE LIPOAMIDE RESIDUES OF THE PYRUVATE DEHYDROGENASE MULTIENZYME COMPLEX OF ESCHERICHIA-COLI.

L7 ANSWER 61 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Regulation of lactate dehydrogenase in Brochothrix thermosphacta

L7 ANSWER 62 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 34
TI MAPPING OF THE S' SUBSITES OF PORCINE PANCREATIC AND HUMAN LEUKOCYTE ELASTASES.

L7 ANSWER 63 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI PHOSPHORUS-31 NMR STUDY OF TRYPTOPHANASE EC-4.1.99.1 PYRIDOXAL PHOSPHATE BINDING SITE.

L7 ANSWER 64 OF 94 MEDLINE on STN DUPLICATE 35
TI Conformations in solution of alpha,alpha-trehalose, alpha-D-glucopyranosyl alpha-D-mannopyranoside, and their 1-thioglycosyl analogs, and a tentative correlation of their behaviour with respect to the enzyme trehalase.

L7 ANSWER 65 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI High field proton nuclear magnetic resonance studies on the active site of subtilisin and thiolsubtilisin

L7 ANSWER 66 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 36
TI NMR STUDIES OF THE NUCLEOTIDE BINDING SITES OF PORCINE ADENYLATE KINASE.

L7 ANSWER 67 OF 94 MEDLINE on STN DUPLICATE 37
TI Substrate and product specificity of Arthrobacter sialophilus neuraminidase.

L7 ANSWER 68 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 38

TI FLUORESCENCE AND NUCLEAR RELAXATION ENHANCEMENT STUDIES OF THE BINDING OF GLUTATHIONE DERIVATIVES TO MANGANESE RECONSTITUTED GLYOXALASE I EC-4.4.1.5 FROM HUMAN ERYTHROCYTES A MODEL FOR THE CATALYTIC MECHANISM OF THE ENZYME INVOLVING A HYDRATED METAL ION.

L7 ANSWER 69 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI A covalent NAD intermediate in the urocanase reaction

L7 ANSWER 70 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI High field proton nuclear magnetic resonance studies on the active site of subtilisin and thiolsubtilisin

L7 ANSWER 71 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI DIRECT OBSERVATION BY NMR OF 2 COEXISTING CONFORMATIONS OF AN ENZYME LIGAND COMPLEX IN SOLUTION.

L7 ANSWER 72 OF 94 MEDLINE on STN DUPLICATE 39
TI Kinetic and magnetic resonance studies of substrate binding to galactose oxidase copper(II).

L7 ANSWER 73 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Synthesis of glycal neuraminidase inhibitors. Part 1. 2,3-Dehydro-4-epi-N-acetylneuraminic acid

L7 ANSWER 74 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI A study of porphyrin analogs. III. Syntheses, enzyme interactions, and self-aggregation of new models for types I, III, and IX porphyrins

L7 ANSWER 75 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI A study of the substrate and inhibitor specificities of AMP aminohydrolase, 5'-nucleotidase, and adenylate kinase with adenosine carboxylates of variable chain length

L7 ANSWER 76 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI STUDIES ON 6 METHYL-5-DEAZA TETRA HYDROPTERIN AND ITS 4A ADDUCTS.

L7 ANSWER 77 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 40
TI HYDROGEN TRITIUM EXCHANGE TITRATION OF THE HISTIDINE RESIDUES IN RNASE T-1 AND ANALYSIS OF THEIR MICRO ENVIRONMENTS.

L7 ANSWER 78 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 41
TI PROTON NMR AND PHOSPHORUS NMR STUDIES OF RNASE T-1 EC-2.7.7.26.

L7 ANSWER 79 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 42
TI THE LOCI OF BINDING OF THE SPECIFIC INHIBITORS METHANOL AND ANILINE TO BOVINE CARBONIC ANHYDRASE.

L7 ANSWER 80 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 43
TI FLUORINE-19 NMR STUDIES OF THE INTERACTION OF INHIBITORS WITH CHYMOTRYPSIN DERIVATIVES OF TRYPTOPHAN AND PHENYL ALANINE.

L7 ANSWER 81 OF 94 MEDLINE on STN DUPLICATE 44
TI [Aminoglycoside-3'-phosphotransferase I from aminoglycoside-polyresistant strain E. coli 182].
Aminoglikozid-3'-fosfotransferaza I iz kletok E. Coli 182 s mnozhestvennoi

ustoichivost'iu k aminoglikozidnym antibiotikam.

L7 ANSWER 82 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Studies of fluorine-19-labeled Met-192-chymotrypsin: an NMR study of an activating moiety near the catalytic serine

L7 ANSWER 83 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 45
TI PURIFICATION AND CHARACTERIZATION OF PYRIDOXAL 5 PHOSPHATE DEPENDENT SERINE HYDROXY METHYLASE EC-2.1.2.1 FROM LAMB LIVER AND ITS ACTION UPON BETA PHENYL SERINES.

L7 ANSWER 84 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Substrate proton exchange catalyzed by γ-cystathionase

L7 ANSWER 85 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 46
TI BINDING OF HYDROGEN DONORS TO HORSERADISH PEROXIDASE EC-1.11.1.7 A SPECTROSCOPIC STUDY.

L7 ANSWER 86 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Monoanion inhibition and chlorine-35 nuclear magnetic resonance studies of renal dipeptidase

L7 ANSWER 87 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Regulation of Escherichia coli glutamine synthetase. Evidence for the action of some feedback modifiers at the active site of the unadenylylated enzyme

L7 ANSWER 88 OF 94 MEDLINE on STN DUPLICATE 47
TI Mandelate racemase from Pseudomonas putida. Magnetic resonance and kinetic studies of the mechanism of catalysis.

L7 ANSWER 89 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Pyruvate carboxylase. Inhibition of the mammalian and avian liver enzymes by α-ketoglutarate and L-glutamate

L7 ANSWER 90 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Intrinsic catalytic activity of the zymogen, bovine procarboxypeptidase A. Kinetic study using fluorine analogs

L7 ANSWER 91 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Analogs of S-adenosylhomocysteine as potential inhibitors of biological transmethylation. Specificity of the S-adenosylhomocysteine binding site

L7 ANSWER 92 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Early interactions between inhibitors and antibodies to lysozyme

L7 ANSWER 93 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Mechanism of the iron(II) activated enzyme, aconitase

L7 ANSWER 94 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
TI Aspartate transcarbamylase. A nuclear magnetic resonance study of the binding of inhibitors and substrates to the catalytic subunit

=> d ibib abs l7, 6,
17,18,34,38,42,44,46,47,53,54,63,65,66,67,68,70,71,72,73,74,75,78,80,82,86,88,89,90,
91,92,93,94

L7 ANSWER 6 OF 94 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1998301373 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9636032
TITLE: Potent peptide inhibitors of human hepatitis C virus NS3 protease are obtained by optimizing the cleavage products.
AUTHOR: Ingallinella P; Altamura S; Bianchi E; Taliani M; Ingenito R; Cortese R; De Francesco R; Steinkuhler C; Pessi A
CORPORATE SOURCE: Istituto di Ricerche di Biologia Molecolare P. Angeletti (IRBM), Rome, Italy.
SOURCE: Biochemistry, (1998 Jun 23) Vol. 37, No. 25, pp. 8906-14.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 31 Jul 1998
Last Updated on STN: 31 Jul 1998
Entered Medline: 20 Jul 1998

AB In the absence of a broadly effective cure for hepatitis caused by hepatitis C virus (HCV), much effort is currently devoted to the search for inhibitors of the virally encoded protease NS3. This chymotrypsin-like serine protease is required for the maturation of the viral polyprotein, cleaving it at the NS3-NS4A, NS4A-NS4B, NS4B-NS5A, and NS5A-NS5B sites. In the course of our studies on the substrate specificity of NS3, we found that the products of cleavage corresponding to the P6-P1 region of the substrates act as competitive inhibitors of the enzyme, with IC50s ranging from 360 to 1 microM. A detailed study of product inhibition by the natural NS3 substrates is described in the preceding paper [Steinkuhler, C., et al. (1997) Biochemistry 37, 8899-8905]. Here we report the results of a study of the structure-activity relationship of the NS3 product inhibitors, which suggest that the mode of binding of the P region-derived products is similar to the ground-state binding of the corresponding substrates, with additional binding energy provided by the C-terminal carboxylate. Optimal binding requires a dual anchor: an "acid anchor" at the N terminus and a "P1 anchor" at the C-terminal part of the molecule. We have then optimized the sequence of the product inhibitors by using single mutations and combinatorial peptide libraries based on the most potent natural product, Ac-Asp-Glu-Met-Glu-Glu-Cys-OH (Ki = 0.6 microM), derived from cleavage at the NS4A-NS4B junction. By sequentially optimizing positions P2, P4, P3, and P5, we obtained several nanomolar inhibitors of the enzyme. These compounds are useful both as a starting point for the development of peptidomimetic drugs and as structural probes for investigating the substrate binding site of NS3 by modeling, NMR , and crystallography.

L7 ANSWER 17 OF 94 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 97092814 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8938376
TITLE: Calystegine B4, a novel trehalase inhibitor from Scopolia japonica.
AUTHOR: Asano N; Kato A; Kizu H; Matsui K; Watson A A; Nash R J
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan.
SOURCE: Carbohydrate research, (1996 Oct 31) Vol. 293, No. 2, pp. 195-204.
Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19 Feb 1997

Last Updated on STN: 19 Feb 1997
Entered Medline: 30 Jan 1997

AB GLC-MS analysis has been developed for screening plants of the family Solanaceae for new calystegines. GLC-MS analyses of the extract of Scopolia japonica showed the presence of a new tetrahydroxy-nor-tropane alkaloid in addition to the known calystegines A3, A5, B1, B2, B3, and C1. We gave this new alkaloid the trivial name calystegine B4. The structure of calystegine B4 was determined as 1 alpha, 2 beta, 3 alpha, 4 alpha-tetrahydroxy-nor-tropane from a variety of NMR spectral data. Calystegines B1, B2, and C1 are potent competitive inhibitors with Ki values ranging from 10(-6) to 10(-7) M for almond beta-glucosidase, while calystegine B4 inhibited this enzyme in a competitive manner, with a Ki value of 7.3 microM. Calystegine B2 is also a potent inhibitor of green coffee bean alpha-galactosidase, whereas calystegine B4 exhibited no significant activity for this enzyme. Among rat intestinal glycosidases, only trehalase was potently inhibited by calystegine B4, with an IC50 value of 9.8 microM. Furthermore, calystegine B4 potently inhibited pig kidney trehalase in a competitive manner, with a Ki value of 1.2 microM, but it was almost inactive against yeast and fungal trehalases.

L7 ANSWER 18 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 8

ACCESSION NUMBER: 1996:218451 BIOSIS
DOCUMENT NUMBER: PREV199698774580
TITLE: Lipoxygenase-1 inhibition with a series of half-product analogs.
AUTHOR(S): Zhu, Zhenyu; Funk, Max O., Jr.
CORPORATE SOURCE: Departments Chemistry Medicinal Biological Chemistry, University Toledo, Toledo, OH 43606, USA
SOURCE: Bioorganic Chemistry, (1996) Vol. 24, No. 1, pp. 95-109. CODEN: BOCMBM. ISSN: 0045-2068.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 1996
Last Updated on STN: 8 May 1996

AB A new series of sulfur-containing competitive inhibitors for lipoxygenase-1 from soybeans has been synthesized and characterized. The compounds resemble the omega-half of the product of catalysis, and can, therefore, be thought of as half-product analogs. A series of inhibitors differing in the length of the omega-terminal aliphatic substituent was assembled. Lipoxygenase-1 inhibition at pH 9 was greatest for (E)-4-thia-2-undecenal, the compound bearing the nC-7H-15 substituent. Longer or shorter aliphatic substituents provided less effective inhibitors. This optimal fit of the inhibitory compounds reflecting the known substrate specificity of the enzyme along with the competitive inhibition kinetics displayed by these substances implicated an active site interaction. The relatively uncomplicated features of the compounds made it possible to explore synthetically for other aspects of the structure favorable for an inhibitory effect. Compounds containing functional groups other than the aldehyde at the 1-position were all less effective inhibitors. In addition to the optimal hydrophobic substituent, an electron-rich region in the molecule was also critical to the inhibitory effect. alpha,beta-Unsaturated aldehydes were about 10 times more effective inhibitors than the saturated analogs. The 4-thia substituent was not absolutely required for inhibition, but electron density at this position was important. gamma,delta-Unsaturation replaced the sulfur in this capacity with little effect on the inhibition constant. The electron-rich aldehydes showed no tendency to form hydrates in aqueous solution or Schiff base adducts with the enzyme. Physical evidence for a protein-ligand interaction was sought in a series of 1H NMR

spectroscopy experiments. There was clear evidence for a specific interaction between the compounds and the enzyme in these measurements.

L7 ANSWER 34 OF 94 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 93003149 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1390760
TITLE: Conformational changes in phospholipase A2 upon binding to micellar interfaces in the absence and presence of competitive inhibitors. A 1H and 15N NMR study.
AUTHOR: Peters A R; Dekker N; van den Berg L; Boelens R; Kaptein R; Slotboom A J; de Haas G H
CORPORATE SOURCE: Bijvoet Center for Biomolecular Research, State University of Utrecht, The Netherlands.
SOURCE: Biochemistry, (1992 Oct 20) Vol. 31, No. 41, pp. 10024-30.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 22 Jan 1993
Last Updated on STN: 6 Feb 1995
Entered Medline: 18 Nov 1992

AB An NMR study has been made of porcine pancreatic phospholipase A2 (PLA) in three environments: free in solution, in a binary complex with dodecylphosphocholine micelles, and in a ternary complex with a micelle and the substrate-like inhibitor (R)-1-octyl-2-(N-dodecanoylamino)-2-deoxyglycero-3-phosph oglycol. 1H and 15N chemical shifts, amide exchange rates, and NOE intensities are compared for the enzyme in different environments. From these data, structural differences are found for the N-terminal part, the end of the surface loop at residues Tyr69 and Thr70, and the active site residue His48, and also for the Ca-binding loop (residues 28-32). Specifically, when binding to a micelle, the side chains of residues Ala1, Trp3, and Tyr69, as well as all protons of Thr70, are found to be closer together. After subsequent introduction of the competitive inhibitor, further changes are found for these residues. The N-terminus is flexible in PLA free in solution, in contrast with the crystal structures where it adopts an alpha-helical conformation. According to the NMR data, this helix is rigidly formed only in the ternary complex. Furthermore, in the ternary complex, the N-terminal amino group and the exchangeable hydrogen at N3 of the ring of His48 are observed. We propose that PLA is activated in two steps. An initial conformational change occurs upon binding to a micellar interface. The catalytically active conformation of the enzyme, which has an extensive network of hydrogen bonds, is formed only when binding a substrate or competitive inhibitor at a lipid-water interface.

L7 ANSWER 38 OF 94 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 93011089 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1396670
TITLE: Studies on ribonucleoside-diphosphate reductase from Escherichia coli. The product dCDP is a competitive inhibitor and functions as a spectroscopic probe for the substrate binding site; demonstration by enzyme kinetics and 1H NMR.
AUTHOR: Shen B; Allard P; Kuprin S; Ehrenberg A
CORPORATE SOURCE: Department of Biophysics, Stockholm University, Arrhenius Laboratory, Sweden.
SOURCE: European journal of biochemistry / FEBS, (1992 Sep 15) Vol. 208, No. 3, pp. 631-4.
Journal code: 0107600. ISSN: 0014-2956.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 22 Jan 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 26 Oct 1992

AB Ribonucleoside-diphosphate reductase (EC 1.17.4.1) from Escherichia coli consists of two protein subunits, R1 of 171.5 kDa and R2 of 86.8 kDa, and catalyzes the reduction of all four common ribonucleoside diphosphates. In a search for ligands that bind weakly to the enzyme active site and may be in fast exchange suitable for NMR studies, we have found that the product dCDP is a competitive inhibitor. Kinetics with CDP as substrate shows Km = 4.8 x 10(-5) M and dCDP inhibits with Ki = 1.6 x 10(-4) M. With an assumed diffusion limited binding rate approximately less than 10(9) M-1s-1, the dissociation rate of dCDP would be approximately less than 10(5) s-1. In 1H-NMR experiments studying linewidths, i.e. spin-spin relaxation, dCDP is indeed demonstrated to be in fast exchange. Enzyme subunit R1 causes a line broadening of dCDP resonances. Unexpectedly less broadening was observed when subunit R2 combined with R1. No paramagnetic interaction from the tyrosyl radical of R2 could be detected. It is concluded that dCDP is a promising NMR probe for studies of active-site properties of the enzyme.

L7 ANSWER 42 OF 94 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 91308130 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1854746
TITLE: Conformation of an enzyme-bound substrate of staphylococcal nuclease as determined by NMR.
AUTHOR: Weber D J; Mullen G P; Mildvan A S
CORPORATE SOURCE: Department of Biological Chemistry, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.
CONTRACT NUMBER: DK28616 (NIDDK)
F32 GM13324 (NIGMS)
RR03518 (NCRR)
SOURCE: Biochemistry, (1991 Jul 30) Vol. 30, No. 30, pp. 7425-37.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 13 Sep 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 27 Aug 1991

AB The dinucleoside phosphodiester dTdA is a slow substrate of staphylococcal nuclease (kcat = 3.8 X 10(-3) s-1) that forms binary E-S and ternary E-M-S complexes with Ca2+, Mn2+, Co2+, and La3+. The enzyme enhances the paramagnetic effects of Co2+ on 1/T1 and 1/T2 of the phosphorus and on 1/T1 of six proton resonances of dTdA, and these effects are abolished by binding of the competitive inhibitor 3',5'-pdTp. From paramagnetic effects of Co2+ on 1/T2 of phosphorus, koff of dTdA from the ternary E-Co(2+)-dTdA complex is greater than or equal to 4.8 X 10(4) s-1 and kon greater than or equal to 1.4 X 10(6) M-1 s-1, indicating the 1/T1 values to be in fast exchange. From paramagnetic effects of enzyme-bound Co2+ on 1/T1 of phosphorus and protons, with use of a correlation time of 1.6 ps on the basis of 1/T1 values at 250 and 600 MHz, 7 metal-nucleus distances and 9 lower-limit metal-nucleus distances are calculated. The long Co2+ to 31P distance of 4.1 +/- 0.9 A, which is intermediate between that expected for direct phosphoryl coordination (3.31 +/- 0.02 A) and a

second sphere complex with an intervening water ligand (4.75 +/- 0.02 A), suggests either a distorted inner sphere complex or the rapid averaging of 18% inner sphere and 82% second sphere complexes and may explain the reduced catalytic activity with small dinucleotide substrates. Seventeen interproton distances and 108 lower limit interproton distances in dTdA in the ternary E-La(3+)-dTdA complex were determined by NOESY spectra at 50-, 100-, and 200-ms mixing times. While metal-substrate and interproton distances alone did not yield a unique structure, the combination of both sets of distances yielded a very narrow range of conformations for enzyme-bound dTdA, which was highly extended, with no base stacking, with high-anti glycosidic torsional angles for dT (64 degrees less than or equal to chi less than or equal to 73 degrees) and dA (66 degrees less than or equal to chi less than or equal to 68 degrees) and predominantly C-2'-endo sugar puckers for both nucleosides. Although the individual nucleosides are like those of B-DNA, their unstacked conformation, which is inappropriate for base pairing, as well as the conformational angles alpha and gamma of dA and zeta of dT, rule out B-DNA.(ABSTRACT TRUNCATED AT 400 WORDS)

L7 ANSWER 44 OF 94 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 91329552 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1651124
TITLE: Proton and tritium NMR relaxation studies of peptide inhibitor binding to bacterial collagenase: conformation and dynamics.
AUTHOR: Dive V; Lai A; Valensin G; Saba G; Yiotakis A; Toma F
CORPORATE SOURCE: Service de Biochimie, Laboratoire d'Ingenierie des Proteines, CEN-Saclay, France.
SOURCE: Biopolymers, (1991 Feb 15) Vol. 31, No. 3, pp. 305-17. Journal code: 0372525. ISSN: 0006-3525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 6 Oct 1991
Last Updated on STN: 6 Oct 1991
Entered Medline: 19 Sep 1991

AB The interaction of succinyl-Pro-Ala, a competitive inhibitor of Achromobacter iophagus collagenase, with the enzyme was studied by longitudinal proton and tritium relaxation. Specific deuterium and tritium labeling of the succinyl part at vicinal positions allowed the measurement of the cross-relaxation rates of individual proton or tritium spin pairs in the inhibitor-enzyme complex as well as in the free inhibitor. Overall correlation times, internuclear distances, and qualitative information on the internal mobility in Sucl (as provided by the generalized order parameter S2) could be deduced by the comparison of proton and tritium cross-relaxation of spin pairs at complementary positions in the -CH2- CH2- moiety as analyzed in terms of the model-free approach by Lipari and Szabo. The conformational and motional parameters of the inhibitor in the free and enzyme-bound state were directly compared by this method. The measurement of proton cross-relaxation in the Ala residue provided additional information on the inhibitor binding. The determination of the order parameter in different parts of the inhibitor molecule in the bound state indicates that the succinyl and alanyl residues are primarily involved in the interaction with the enzyme activity site. The succinyl moiety, characterized in solution by the conformational equilibrium among the three staggered rotamers--i.e., trans: 50%; g+: 20%; g-: 30%--adopted in the bound state the unique trans conformation.

L7 ANSWER 46 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:590189 CAPLUS
DOCUMENT NUMBER: 111:190189
TITLE: Dehydroquinate synthase: the use of substrate analogs to probe the late steps of the catalyzed reaction
AUTHOR(S): Widlanski, Theodore; Bender, Steven L.; Knowles, Jeremy R.
CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: Biochemistry (1989), 28(19), 7572-82
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The later steps of the proposed mechanistic pathway for the reaction catalyzed by dehydroquinate synthase were probed by using 3 substrate analogs. Each of these analogs was structurally prohibited from undergoing the ring-opening reaction that necessarily precedes the C-C bond-forming step in the overall conversion of the substrate 3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) to dehydoquinate. Two of the analogs [the 2-deoxy cyclic compound (I) and the carbacyclic analog (II)] were locked into a cyclic form, mimicking the pyranose form of the substrate, DAHP. The 3 analog (III) contained no carbonyl group at C-2 and may thus resemble the open-chain form of DAHP. Analogs I and II each bound to the enzyme and were competitive inhibitors with Ki values of 35 and 0.12 μM, resp. More importantly, however, incubation of these analogs with the enzyme led to the catalytic production of phosphate along with the corresponding exomethylene compds. that were analogous to the enol ether intermediate postulated for the normal synthase reaction. In contrast to these results, acyclic analog III was neither a substrate nor an inhibitor of the enzyme. These data suggested that the enzyme recognizes and acts upon the α-pyranose form of the natural substrate. The ready release of the exomethylene products from the processing of analogs I and II was consistent with a previous suggestion that the enzyme may release the enol ether intermediate into solution, where the ring opening and cyclization occur nonenzymically. The use of I stereospecifically labeled with deuterium at C-7 allowed the stereochem. course of the β-elimination of phosphate to be established. This step proceeds with syn stereochem., which fit the pattern of enzyme-catalyzed elimination from substrates where the proton is lost from a position α to a ketone or thiol ester. Since the overall stereochem. course of the transformation mediated by dehydroquinate synthase had been shown to be inversion, the present finding of a syn elimination suggests that the transition state for the subsequent intramol. aldol reaction has a chairlike geometry.

L7 ANSWER 47 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 26
ACCESSION NUMBER: 1989:385206 BIOSIS
DOCUMENT NUMBER: PREV198988065796; BA88:65796
TITLE: SULFOXIMINE AND SULFODIIMINE TRANSITION-STATE ANALOGUE INHIBITORS FOR CARBOXYPEPTIDASE A.
AUTHOR(S): MOCK W L [Reprint author]; TSAY J-T
CORPORATE SOURCE: DEP CHEM, UNIV ILLINOIS CHICAGO, CHICAGO, ILL 60680, USA
SOURCE: Journal of the American Chemical Society, (1989) Vol. 111, No. 12, pp. 4467-4472.
CODEN: JACSAT. ISSN: 0002-7863.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 17 Aug 1989
Last Updated on STN: 23 Sep 1989

AB New substrate analogues [(Λ)-2-carboxy-3-phenylpropyl]methylsulfoximine and [(-)-2-carboxy-3-phenylpropyl]methylsulfodiimine have been prepared and shown to be potent

competitive inhibitors of the zinc enzyme carboxypeptidase A (limiting values of Ki = 2.7 and 0.22 μM, respectively). A complicated pH dependence for Ki is explained by deprotonations occurring on the enzyme, the inhibitor, and the enzyme-inhibitor complex. The mode of inhibitor binding is also characterized by visible absorption and 1H NMR spectra of the cobalt-substituted enzyme. Mechanistic consequences are considered; no support is found for a concerted mechanism of acyl substitution occurring within the coordination sphere of the active-site metal ion.

L7 ANSWER 53 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:529409 CAPLUS
DOCUMENT NUMBER: 111:129409
TITLE: NMR studies of enzyme inhibition
AUTHOR(S): Thomas, W. Anthony; Whitcombe, Ian W. A.; Williamson, Michael P.
CORPORATE SOURCE: Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK
SOURCE: Alfred Benzon Symposium (1988), Volume Date 1987, 26(NMR Spectrosc. Drug Res.), 40-56
CODEN: ABSYB2; ISSN: 0105-3639
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 14 refs., of applications of high-field NMR techniques in the design of competitive inhibitors of enzymes thought to be involved in disease states, including angiotensin-converting enzyme, phospholipase A2, and collagenase.

L7 ANSWER 54 OF 94 MEDLINE on STN DUPLICATE 29
ACCESSION NUMBER: 87271570 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3038164
TITLE: Lysophosphatidylcholines containing polyunsaturated fatty acids were found as Na+, K+-ATPase inhibitors in acutely volume-expanded hog.
AUTHOR: Tamura M; Harris T M; Higashimori K; Sweetman B J; Blair I A; Inagami T
CONTRACT NUMBER: GM-15431 (NIGMS)
HL14192 (NHLBI)
HL35323 (NHLBI)
+
SOURCE: Biochemistry, (1987 May 19) Vol. 26, No. 10, pp. 2797-806.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 31 Aug 1987
AB Na+, K+-ATPase inhibitors possessing inhibitory activities against the specific binding of ouabain to Na+, K+-ATPase and 86Rb uptake into hog erythrocytes have been purified from the plasma of acutely saline-infused hog. The purifications were performed by a combination of Amberlite XAD-2 adsorption chromatography and four steps of high-performance liquid chromatography with four different types of columns. Fast atom bombardment (FAB) mass and proton NMR spectrometric studies identified the purified substances as gamma-arachidoyl- [LPCA(gamma), 34%], beta-arachidoyl- [LPCA(beta), 4%], gamma-linoleoyl- (LPCL, 33%), and gamma-oleoyl- (LPCO, 25%) lysophosphatidylcholine, expressed in molar ratio in the plasma. Small amounts of gamma-docosapentaenoyl-,

gamma-eicosatrienoyl-, and gamma-palmitoyllysophosphatidylcholine were also detected by both FAB mass and 1H NMR spectrometric studies. Only gamma-acyl-LPC's showed inhibitory activities on Na+,K+-ATPase and ouabain-binding activities. These LPC's were effective at 100 microM levels in attaining 50% inhibition of the enzyme activity. The inhibition of Na+,K+-ATPase activity due to these compounds was always more sensitive than that of both ouabain-binding and 86Rb uptake activities. The ouabain-displacing activity in plasma due to these compounds increased with time during saline infusion. The maximal plasma level was approximately 10 times higher than that in the preinfusion plasma sample. Although these results suggest the gamma-acyl-LPC's with long-chain polyunsaturated fatty acids are not simple competitive inhibitors to Na+, K+ -ATPase, these compounds could be implicated in the pathogenesis of the circulation abnormality through the modulation of membrane enzyme.

L7 ANSWER 63 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1983:317801 BIOSIS
DOCUMENT NUMBER: PREV198376075293; BA76:75293
TITLE: PHOSPHORUS-31 NMR STUDY OF TRYPTOPHANASE EC-4.1.99.1 PYRIDOXAL PHOSPHATE BINDING SITE.
AUTHOR(S): SCHNACKERZ K D [Reprint author]; SNELL E E
CORPORATE SOURCE: INST PHYSIOL CHEM, UNIV WUERZBURG MED SCH, D-8700 WUERZBURG, W GER
SOURCE: Journal of Biological Chemistry, (1983) Vol. 258, No. 8, pp. 4839-4841.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The pyridoxal phosphate-dependent enzyme tryptophanase [from Escherichia coli] was investigated using 31P NMR at 72.86 MHz. In the native enzyme, the pyridoxal-P 31P chemical shift was 3.55 ppm and independent of pH, indicating that the dianionic phosphate group of the cofactor is not accessible to solvent. Binding of the competitive inhibitor, β-phenyl-DL-serine, results in the formation of the transaldimination complex. This complex is fixed to the enzyme via the dianionic phosphate group of the cofactor; again, the observed shift is independent of pH. In both cases, restricted rotational freedom of the phosphate group around the C.sbd.O bond linking the phosphate ester to the pyridine moiety of the cofactor could be asserted from line width data. Addition of the competitive inhibitor, L-alanine, to tryptophanase produces the quinonoid intermediate. The phosphate group of this complex lost its specific interaction (probably a salt bridge) with the protein, as indicated by the pH dependence of the chemical shift.

L7 ANSWER 65 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:606717 CAPLUS
DOCUMENT NUMBER: 101:206717
TITLE: High field proton nuclear magnetic resonance studies on the active site of subtilisin and thiolsubtilisin
AUTHOR(S): Jordan, Frank; Polgar, Laszlo; Guillermo, Tous
CORPORATE SOURCE: Dep. Chem., Rutgers, State Univ., Newark, NJ, 071202, USA
SOURCE: Kemiai Kozlemenyek (1983), 60(1-2), 143-54
CODEN: KEKOAS; ISSN: 0022-9814
DOCUMENT TYPE: Journal
LANGUAGE: Hungarian

AB The very-low-field 1H NMR resonance found in aqueous solns. of serine proteases is characteristic of the H-bond between the imidazolium and aspartate groups of the catalytic triad, serine-histidine

(His)-aspartate (Asp). No such resonance was found in native subtilisins (even at -2° and pH 6.0), but was present in thiolsubtilisins and in the phenylboronic acid derivs. of the serine enzymes. The His at the catalytic site of thiosubtilisin carries a pos. charge at pH 5.6-8.4, implying the existence of a mercaptide-imidazolium ion-pair at the catalytic site. A stable H-bond found between Asp and His in the thiol enzyme and in the phenylboronic acid derivative of the serine enzyme probably exists and is likely most important in the tetrahedral transition state formed between the serine enzyme and its substrate and bearing a similar (- + -) charge distribution. The stereochem. requirements for creation of such a charge distribution were demonstrated: subtilisin with saturating N-acetyl-L-tryptophan gave rise to the said resonance, but not with N-acetyl-D-tryptophan and L-tryptophanamide (all 3 are competitive inhibitors of the serine enzyme). The pH dependence of the area of the resonance in the presence of N-acetyl-L-tryptophan suggests a pK near 7 for the catalytic His. The dependence of the chemical shifts of the His C2-H in subtilisin (including that at the catalytic site), indicate that all possess pK values of 7.

L7 ANSWER 66 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 36

ACCESSION NUMBER: 1983:268040 BIOSIS
DOCUMENT NUMBER: PREV198376025532; BA76:25532
TITLE: NMR STUDIES OF THE NUCLEOTIDE BINDING SITES OF PORCINE ADENYLATE KINASE.
AUTHOR(S): SMITH G M [Reprint author]; MILDVAN A S
CORPORATE SOURCE: DEP PHYSIOLOGICAL CHEMISTRY, JOHNS HOPKINS MED SCH, BALTIMORE, MD 21205, USA
SOURCE: Biochemistry, (1982) Vol. 21, No. 24, pp. 6119-6123. CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The α,β,γ-tridentate complex of CrATP, a paramagnetic competitive inhibitor of porcine adenylate kinase, increases the longitudinal [1/(fT1p)] and transverse [1/(fT2p)] relaxation rates of a resonance of the enzyme previously assigned to the C2 proton of histidine-36. These paramagnetic effects are diminished upon the addition of the substrate MgATP by an amount consistent with the simple displacement of CrATP. The 1/(fT2p) value sets a lower limit of 400 s-1 on the rate constant for dissociation of CrATP from the enzyme. The 1/(fT1p) value at 250 MHz and the correlation time for water protons in the same complex are used to calculate a distance of 12.9 ± 1.0 Å from Cr(III) to the C2 proton of histidine-36. A primary, negative nuclear Overhauser effect is detected on the adenine H2 resonance of enzyme-bound MgATP upon preirradiation of the C2 proton of histidine-36, indicating that these protons are .ltorsim. 5 Å apart. These distances and negative intramolecular Overhauser effects from the ribose protons to adenine H8 of MgATP indicate an extended structure for bound MgATP with an anti-conformation about the glycosidic bond. These findings require a different orientation or location of the bound metal-ATP substrate from that proposed based on X-ray studies of the binding of salicylate. Other nuclear Overhauser effects from resonances of the protein at 1.8 and 0.9 ppm to both adenine H2 and ribose H1' of bound MgATP indicate the proximity to the substrate of at least 1 Arg Cβ proton (at 1.8 ppm), Cγ proton (at 1.7 ppm), Lys Cδ proton (at 1.7 ppm), or Leu Cβ proton (at 1.6 ppm) and 1 or more Leu, Ile, or Val methyl groups (at 0.9 ppm). Entirely different Overhauser effects are observed from the enzyme to the adenine protons of AMP consistent with a distinct site for the other substrate.

L7 ANSWER 67 OF 94 MEDLINE on STN DUPLICATE 37

ACCESSION NUMBER: 82167626 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7068676
TITLE: Substrate and product specificity of Arthrobacter sialophilus neuraminidase.
AUTHOR: Kessler J; Heck J; Tanenbaum S W; Flashner M
CONTRACT NUMBER: R0I-AI-12532-06 (NIAID)
RR07174 (NCRR)
SOURCE: The Journal of biological chemistry, (1982 May 10) Vol. 257, No. 9, pp. 5056-60.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198206
ENTRY DATE: Entered STN: 17 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 24 Jun 1982

AB Arthrobacter sialophilus neuraminidase catalyzes the hydrolysis of N-acetylneuraminyl-alpha-oxygen, nitrogen, and azido glycosides. The most effective of those substrates examined was N-acetylneuraminyl-alpha-4-methylumbelliferylglycoside (AcNeu-alpha-4-MU; Km app, 0.0193 mM; kcat, 136.4 sec-1). The products resulting from the enzymic hydrolysis of N-acetylneuraminyl-alpha-azido-glycoside were N-acetylneuraminic acid and azide ion. N-acetylneuraminyl-alpha-2,3-thiogalactylglycoside and N-acetylneuraminyl-alpha-2,6-thiogalactylglycoside were competitive inhibitors of the enzyme having KI values of 1.52 mM and 1.70 mM, respectively. Dissociation constants for these thioglycosides were also determined by fluorescence enzyme titrations which gave values similar to those determined kinetically. N-Acetylneuraminic acid, but not its methyl ester, was a competitive inhibitor of neuraminidase. Its KI value, 0.18 mM, was also determined by both methods. 5-Acetamido-2,6-anhydro-3,5-dideoxy-D-glycero-D-talo-nonulosonic acid (2-deoxy-4-epi-AcNeu) was found to be a weak competitive inhibitor (KI, 12.1 mM). A. sialophilus neuraminidase further catalyzes transglycosidation reactions with methanol as acceptor. Methanol had no effect on the release of 4-MU by enzymatic hydrolysis of AcNeu-alpha-4-MU, suggesting that the formation of the enzyme-glycone intermediate is the rate-determining step. The anomeric configuration of the product of this reaction, as shown by 13C-nmr spectroscopy, is N-acetylneuraminyl-alpha-methylglycoside. Neuraminidase, therefore, catalyzes its reactions with overall retention of configuration.

L7 ANSWER 68 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 38
ACCESSION NUMBER: 1983:204509 BIOSIS
DOCUMENT NUMBER: PREV198375054509; BA75:54509
TITLE: FLUORESCENCE AND NUCLEAR RELAXATION ENHANCEMENT STUDIES OF THE BINDING OF GLUTATHIONE DERIVATIVES TO MANGANESE RECONSTITUTED GLYOXALASE I EC-4.4.1.5 FROM HUMAN ERYTHROCYTES A MODEL FOR THE CATALYTIC MECHANISM OF THE ENZYME INVOLVING A HYDRATED METAL ION.
AUTHOR(S): SELLIN S [Reprint author]; ERIKSSON L E G; MANNERVIK B
CORPORATE SOURCE: DEP BIOCHEM, ARRHENIUS LAB, UNIV STOCKHOLM, S-106 91 STOCKHOLM, SWEDEN
SOURCE: Biochemistry, (1982) Vol. 21, No. 20, pp. 4850-4857.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The apoenzyme of glyoxalase I (EC 4.4.1.5) from human erythrocytes was prepared by removal of Zn2+ with EDTA. Methanol was used as a stabilizing

agent. Extended dialysis was required to remove EDTA from the resulting solution of apoenzyme. Reconstitution with Mn2+ was followed by measuring enzyme activity, EPR of free Mn2+ ions and NMR of water protons. The holoenzyme contained 2 Mn2+/protein dimer and had .apprx. 50% of the catalytic activity of the native enzyme. The binding of the cosubstrate glutathione (γ-L-glutamyl-L-cysteinylglycine), the product S-D-lactoylglutathione and the competitive inhibitor S-(p-bromobenzyl)glutathione was monitored by the quenching of the intrinsic tryptophan fluorescence and by the proton relaxation enhancement of water bound to Mn2+ in the active site of the enzyme. Kd were 1.1 mM, 0.42 mM and 0.54 μM for glutathione, S-D-lactoylglutathione and S-(p-bromobenzyl)glutathione, respectively. The temperature and frequency dependences of the longitudinal and transverse paramagnetic relaxation rates, 1/T1p and 1/T2p, were studied for water. The results were analyzed in terms of correlation and exchange times. Proton and deuteron relaxation rates were measured in parallel at 2 different magnetic fields. Good agreement between the 2 approaches of analysis was noticed. Two water molecules are bound in the 1st coordination sphere of Mn2+ in the active site of glyoxalase I. When S-(p-bromobenzyl)glutathione or S-D-lactoylglutathione is bound to the enzyme, only 1 exchangeable water molecule could be detected, indicating occlusion of the 2nd water molecule. An enediol mechanism involving the metal-bound water is proposed for the catalysis effected by glyoxalase I.

L7 ANSWER 70 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:522924 CAPLUS
DOCUMENT NUMBER: 97:122924
TITLE: High field proton nuclear magnetic resonance studies on the active site of subtilisin and thiolsubtilisin
AUTHOR(S): Jordan, F.; Polgar, L.; Tous, G.
CORPORATE SOURCE: Dep. Chem., Rutgers, State Univ., Newark, NJ, 07102, USA
SOURCE: Studies in Physical and Theoretical Chemistry (1982), 18(Steric Eff. Biomol.), 271-89
CODEN: SPTCDZ; ISSN: 0167-6881
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The very low field 1H NMR resonance found in aqueous solns. of serine proteases (characteristic of the H bond between the imidazolium and aspartate groups of the catalytic triad serine...histidine...aspartic acid) was not found in native subtilisins even at -2° and pH 6.0. This resonance was present in thiolsubtilisins and in the phenylboronic acid derivs. of the serine enzymes. The histidyl residue at the catalytic site of thiolsubtilisin carries a pos. charge at pH 5.6-8.4, implying the existence of a mercaptide-imidazolium ion pair at the catalytic site. The stable H bond found between the aspartyl and histidyl residues in the thiolenzyme and in the phenylboronic acid derivative of the serine enzyme probably exists and is probably most important in the tetrahedral transition state formed between the serine enzyme and its substrate and bearing a similar - + - charge distribution. The stereochem. requirements for creation of such a charge distribution were demonstrated: subtilisin with saturating N-acetyl-L-tryptophan gave rise to this resonance, whereas N-acetyl-D-tryptophan and L-tryptophanamide did not (all 3 are competitive inhibitors of the serine enzyme). The pH dependence of the area of the resonance in the presence of N-acetyl-L-tryptophan suggests a pK of .apprx.7 for the catalytic histidyl residue. The pH dependence of the chemical shifts of the histidyl C2-H atoms in subtilisins (including that at the catalytic site), indicate that all possess pKas of 7.

L7 ANSWER 71 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1981:248849 BIOSIS
DOCUMENT NUMBER: PREV198172033833; BA72:33833
TITLE: DIRECT OBSERVATION BY NMR OF 2 COEXISTING CONFORMATIONS OF AN ENZYME LIGAND COMPLEX IN SOLUTION.
AUTHOR(S): GRONENBORN A [Reprint author]; BIRDSALL B; HYDE E I; ROBERTS G C K; FEENEY J; BURGEN A S V
CORPORATE SOURCE: DIV MOL PHARMACOL, NATL INST MED RES, LONDON NW7 1AA, UK
SOURCE: Nature (London), (1981) Vol. 290, No. 5803, pp. 273-274. CODEN: NATUAS. ISSN: 0028-0836.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

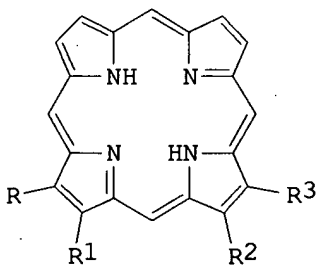
AB Dihydrofolate reductase is the site of action of the anti-folate drugs, e.g., methotrexate, pyrimethamine and trimethoprim, which act as competitive inhibitors of the enzyme. These inhibitors bind to the Lactobacillus casei enzyme cooperatively with the coenzyme NADP(H), which can increase inhibitor binding by as much as 700-fold. The existence of conformational changes accompanying ligand binding and involved in inhibitor-coenzyme cooperativity was inferred from NMR experiments. These conformational changes may be important in determining the specificity of the enzyme for its ligands. Two distinct conformations of the enzyme-trimethoprim-NADP+ ternary complex in solution were directly observed by NMR.

L7 ANSWER 72 OF 94 MEDLINE on STN DUPLICATE 39
ACCESSION NUMBER: 81266232 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6267193
TITLE: Kinetic and magnetic resonance studies of substrate binding to galactose oxidase copper(II).
AUTHOR: Winkler M E; Bereman R D; Kurland R J
SOURCE: Journal of inorganic biochemistry, (1981 Jun) Vol. 14, No. 3, pp. 223-35.
Journal code: 7905788. ISSN: 0162-0134.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198110
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 29 Jan 1999
Entered Medline: 14 Oct 1981

AB Alcohol substrate binding to the copper-containing enzyme galactose oxidase (GOase) has been studied by kinetic competition against cyanide and fluoride, 13C nmr relaxation, and esr competition experiments. The 13C nmr spectra of the substrate beta-O-methyl-D-galactopyranoside (beta-O-me-gal) show no apparent paramagnetic relaxation rate enhancement that could be attributed to innersphere equatorial binding of this molecule at the Cu(II) center. Moreover, the kinetics observed when CN- or F- are used as inhibitors of GOase with beta-O-me-gal as the substrate suggest that these anions act as apparent non-competitive inhibitors; the binding of the substrates beta-O-me-gal and O2 is not hindered per se, but the catalytic activity of the enzyme substrate complex is greatly decreased. The esr competition data also confirm that, in the absence of O2, CN- and beta-O-me-gal do not compete for the same GOase binding site. Previously reported esr and 19F nmr data show that CN- binds to the GOase Cu(II) at an equatorial coordination site, as does the F- detected in esr experiments. Thus, the results from the various competition experiments supports a model in which alcohol substrates bind outersphere to the GOase Cu(II), or, possibly, to an axial site.

L7 ANSWER 73 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:515900 CAPLUS
DOCUMENT NUMBER: 95:115900
TITLE: Synthesis of glycal neuraminidase inhibitors. Part 1. 2,3-Dehydro-4-epi-N-acetylneuraminic acid
AUTHOR(S): Kumar, Virendra; Kessler, Jack; Scott, Mary E.; Patwardhan, Bhalchandra; Tanenbaum, Stuart W.; Flashner, Michael
CORPORATE SOURCE: Coll. Environ. Sci. For., State Univ. New York, Syracuse, NY, 13210, USA
SOURCE: Carbohydrate Research (1981), 94(2), 123-30
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of N-acetylneuraminic acid Me ester with H2SO4 and Ac2O at 50° followed by deacetylation gave 2,3-dehydro-2-deoxy-N-acetylneuraminic acid Me ester and Me 5-acetamido-2,6-anhydro-2,3,5-trideoxy-D-glycero-D-talo-non-2-enonate (2,3-dehydro-4-epi-NeuAc Me ester) in equal yields (.apprx.40% each). The structure of the latter was ascertained primarily from anal. of its mass spectrum, and 1H- and 13C-NMR spectra. The relative proportions of these 2 glycals in the foregoing reaction was dependent on temperature, as at 0°, the yield of 2,3-dehydro-4-epi-NeuAc was markedly diminished. A minor by-product of this acetylation was 2-methyl-(methyl 7,8,9-tri-O-acetyl-2,6-anhydro-2,3,5-trideoxy-D-glycero-D-talo-non-2-enonate)-[4,5-d]-2-oxazoline. Based upon this finding and addnl. interconversion expts., a mechanism involving the intermediacy of the latter oxazoline to account for the epimerization is proposed. These glycals and their Me esters are competitive inhibitors of Arthrobacter sialophilus, neuraminidase, suggesting that the 4-OH group must be equatorially oriented for maximal enzyme inhibition.

L7 ANSWER 74 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:15698 CAPLUS
DOCUMENT NUMBER: 94:15698
TITLE: A study of porphyrin analogs. III. Syntheses, enzyme interactions, and self-aggregation of new models for types I, III, and IX porphyrins
AUTHOR(S): Honeybourne, Colin L.; Jackson, J. Timothy; Simmonds, Derek J.; Jones, Owen T. G.
CORPORATE SOURCE: Phys. Chem. Lab., Bristol Polytech., Bristol, UK
SOURCE: Tetrahedron (1980), 36(12), 1833-8
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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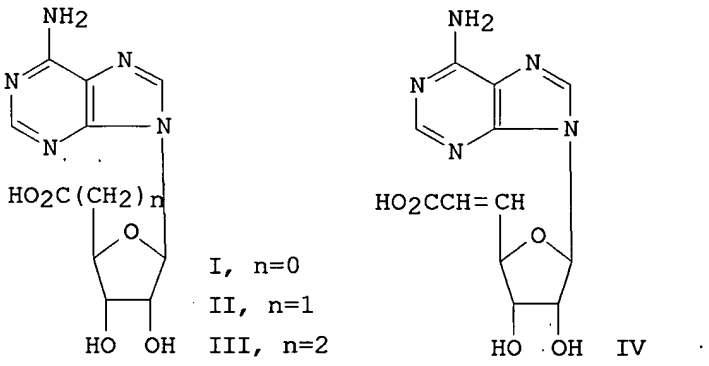
AB The 3 porphyrins I (R, R3 = Me, R1,R2 = (CH2)2CO2Me; R1,R3 = Me, R,R2 = (CH2)2CO2Me; R1,R2 = Me, R,R3 = (CH2)2CO2Me) (II, III, and IV, resp.) were

prepared and their interaction with the mitochondrial enzyme Ferrochelatase were studied. II is the best substrate yet found for Ferrochelatase, with a Michaelis constant of 5.0μM and a maximum rate of 2.8 nmol/min/mg protein, whereas III and IV act as a poor enzyme substrate and as a competitive inhibitor to II, resp. The 1H NMR spectra of these compds. and their zinc(II)bis-pyrrolidine adducts differed considerably, indicating aggregation of the porphyrins. The results for α-meso and γ-meso protons were unusual, and showed that aggregation occurred with electronic effects dominating steric effects.

L7 ANSWER 75 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:402896 CAPLUS
DOCUMENT NUMBER: 93:2896
TITLE: A study of the substrate and inhibitor specificities of AMP aminohydrolase, 5'-nucleotidase, and adenylate kinase with adenosine carboxylates of variable chain length
AUTHOR(S): Meyer, Wilfried; Follmann, Hartmut
CORPORATE SOURCE: Fachber. Chem., Philipps-Univ. Marburg, Marburg, D-3550, Fed. Rep. Ger.
SOURCE: Zeitschrift fuer Naturforschung, C: Journal of Biosciences (1980), 35C(3-4), 273-8
CODEN: ZNCBDA; ISSN: 0341-0382
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A series of AMP analogs in which a terminal carboxylate residue, linked to C4' of the ribose moiety of adenosine by 0, 1, or 2 methylene groups (I, II, and III, resp.) or by the unsatd. ethylidene link (IV) replaced the phosphate anion, was tested for activity as substrates or effectors of 3 enzymes known to interact with AMP with a different degree of specificity. II, III, and IV were substrates of AMP aminohydrolase, III and IV were competitive inhibitors of adenylate kinase, and all acids produced competitive inhibition of the least specific enzyme, 5'-nucleotidase. These activities could be correlated with the intramol. flexibility of anionic substituent and adenine base which in turn was expressed in typical shifts of the NMR signal of purine H-8. The uronic acid, I, having a rigid mol. conformation, was inactive towards 2 AMP-dependent enzymes and hardly active with the 3rd, indicating that this type of compound is not suitable as a nucleotide antagonist, whereas nucleoside carboxylates of types II and III have a higher potential as effectors of nucleotide metabolism

L7 ANSWER 78 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 41

ACCESSION NUMBER: 1979:193113 BIOSIS
DOCUMENT NUMBER: PREV197967073113; BA67:73113
TITLE: PROTON NMR AND PHOSPHORUS NMR STUDIES OF RNASE T-1 EC-2.7.7.26.
AUTHOR(S): ARATA Y [Reprint author]; KIMURA S; MATSUO H; NARITA K
CORPORATE SOURCE: DEP CHEM, UNIV TOKYO, HONGO, TOKYO, JPN
SOURCE: Biochemistry, (1979) Vol. 18, No. 1, pp. 18-24.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB 1H and 31P NMR studies of RNase T1 (EC 2.7.7.26) are reported. Assignments of the C2-H proton resonances of the 3 histidine residues were made using a 3H-labeling technique, a combination of differential 3H-exchange at the C2-H position of histidine and 1H NMR of a differentially 2H-protein. 1H NMR data taken in the absence and presence of 3'-GMP, a strong competitive inhibitor to the enzyme, were used along with 31P NMR spectra of the inhibitor to provide information on the structure of the active site of the enzyme. Apparently histidine-40 along with a carboxyl group which is probably that of glutamic acid-58 is responsible for the catalytic action of the enzyme. The structure of the active site of RNase T1 is in a marked contrast with that of RNase A where 2 histidine residues act as a general acid and general base to conduct the catalytic action. Interaction involving histidine-92 and N-7 of 3'-GMP through a H bond is probably responsible for the enzyme-inhibitor binding. A scheme of the active site and of the interaction of the enzyme with 3'-GMP is presented based on experimental results.

L7 ANSWER 80 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 43

ACCESSION NUMBER: 1979:160964 BIOSIS
DOCUMENT NUMBER: PREV197967040964; BA67:40964
TITLE: FLUORINE-19 NMR STUDIES OF THE INTERACTION OF INHIBITORS WITH CHYMOTRYPSIN DERIVATIVES OF TRYPTOPHAN AND PHENYL ALANINE.
AUTHOR(S): NICHOLSON B C [Reprint author]; SPOTSWOOD T M
CORPORATE SOURCE: ORGAN CHEM DEP, UNIV ADELAIDE, PO BOX 498, ADELAIDE, S AUST 5001, AUST
SOURCE: Australian Journal of Chemistry, (1978) Vol. 31, No. 10, pp. 2167-2178.
CODEN: AJCHAS. ISSN: 0004-9425.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The binding of the inhibitors N-trifluoroacetyltryptophan, N-trifluoroacetylphenylalanine, N-acetyltryptophan and N-acetylphenylalanine to chymotrypsin was studied by 19F NMR spectroscopy at several pH values. Methods for determining the binding parameters, KI and ΔB, including a model for enzyme oligomerization and competitive inhibition from a second inhibitor, are discussed and a general non-linear least-squares method is presented. Values of KI and ΔB are recorded for D and L enantiomers of tryptophan derivatives and for D-phenylalanine derivatives. The results are discussed in terms of a model for the aromatic binding site of chymotrypsin.

L7 ANSWER 82 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1979:82938 CAPLUS
DOCUMENT NUMBER: 90:82938

TITLE: Studies of fluorine-19-labeled Met-192-chymotrypsin: an NMR study of an activating moiety near the catalytic serine
AUTHOR(S): Berliner, Lawrence J.; Landis, Bryan H.
CORPORATE SOURCE: Dep. Chem., Ohio State Univ., Columbus, OH, USA
SOURCE: Jerusalem Symposia on Quantum Chemistry and Biochemistry (1978), 11(Nucl. Magn. Reson. Spectrosc. Mol. Biol.), 311-22
CODEN: JSQCA7; ISSN: 0075-3696
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chymotrypsin labeled at methionine-192 with 19F-labeled o-, m-, or p-(trifluoromethyl)bromoacetanilides was subjected to 19F NMR and kinetic studies. Minor autolyzed forms of the enzyme were easily resolved in the NMR spectra and were removed by chromatog. on Whatman CM-52. The reversible inhibitor, indole, caused an upfield shift of the native peak of labeled enzyme at pH 4.2 consistent with competitive displacement of the trifluoromethyl aromatic group by indole. Dioxane, which also binds in the tosyl pocket, gave similar NMR changes. At pH 5.7, a completely different set of chemical shifts induced by indole were obtained, reflecting the dimerization of chymotrypsin at this pH. Kinetic studies of the enzyme derivs. with specific and nonspecific chymotrypsin substrates along with NMR data allowed calcn. of the partitioning constant between binding of the trifluoromethyl moiety in and out of the tosyl pocket as well as the resp. chemical shifts for these 2 extreme states.

L7 ANSWER 86 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:14041 CAPLUS
DOCUMENT NUMBER: 84:14041
TITLE: Monoanion inhibition and chlorine-35 nuclear magnetic resonance studies of renal dipeptidase
AUTHOR(S): Ferren, Larry G.; Ward, Raymond L.; Campbell, Benedict J.
CORPORATE SOURCE: Biochem. Dep., Univ. Missouri, Columbia, MO, USA
SOURCE: Biochemistry (1975), 14(24), 5280-5
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kinetic analyses of monoanion inhibition and 35Cl NMR at 5.88 MHz were employed to study monoanion interactions with the Zn metalloenzyme, renal dipeptidase. The enzyme-catalyzed hydrolysis of glycyldehydrophenylalanine exhibited competitive inhibition when the reaction rate was determined in the presence of the monovalent anions Fl-, Cl-, Br-, I-, N3-, NO3-, or CNS- or upon the addition of the divalent anion, SO42-. Competitive inhibition was produced by these anions. One anion was bound/enzyme mol., and except in the case of Fl- all of the anions appeared to bind at the same site. Cn- produced a much more effective inhibition of renal dipeptidase than the other monoanions; 2 CN- were bound/enzyme mol. An investigation of the effect of pH upon monoanion inhibition suggested that the anion inhibitors bind to the group with a pK of approx. 7.8. Complete dissociation of this group (.apprx.pH 8.4) eliminated the inhibitory effect of anions. The 35Cl line broadening produced by renal dipeptidase in 0.5M NaCl solns. was 100-fold more effective than that produced by equivalent concns. of aquo-Zn (II). The line broadening was dependent upon the concentration of the metalloenzyme and independent of the frequency of the exciting radiation. When Zn2+ was removed from the metalloenzyme by dialysis or when Cl- was titrated from the metalloenzyme by CN-, line broadening was decreased. Treatment of renal dipeptidase with saturating concns. of the competitive inhibitor, GTP in the presence of 0.5M NaCl also produced a significant decrease in the 35Cl

line width. The 35Cl line broadening produced by renal dipeptidase decreased with increasing pH from 5.8 to 10.8. This line-width variation with pH appeared to result from the titration of a site on the metalloprotein with an approx. pK of 7.4. Temperature studies of 35Cl line broadening by the metalloenzyzme in the presence of Cl and Cn inhibitors suggest that the fast exchange process pertains and that the dominant relaxation mechanism is quadrupolar in nature.

L7 ANSWER 88 OF 94 MEDLINE on STN DUPLICATE 47
ACCESSION NUMBER: 75127935 MEDLINE
DOCUMENT NUMBER: PubMed ID: 164210
TITLE: Mandelate racemase from Pseudomonas putida. Magnetic resonance and kinetic studies of the mechanism of catalysis.
AUTHOR: Maggio E T; Kenyon G L; Mildvan A S; Hegeman G D
SOURCE: Biochemistry, (1975 Mar 25) Vol. 14, No. 6, pp. 1131-9. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197507
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 7 Jul 1975

AB The interactions of mandelate racemase with divalent metal ion, substrate, and competitive inhibitors were investigated. The enzyme was found by electron paramagnetic resonance (EPR) to bind 0.9 Mn2+ ion per subunit with a dissociation constant of 8 muM, in agreement with its kinetically determined activator constant. Also, six additional Mn2+ ions were found to bind to the enzyme, much more weakly, with a dissociation constant of 1.5 mM. Binding to the enzyme at the tight site enhances the effect of Mn2+ on the longitudinal relaxation rate (1/T1p) of water protons by a factor of 11.9 at 24.3 MHz. From the frequency dependence of 1/T1p, it was determined that there are similar to 3 water ligands on enzyme-bound Mn2+ which exchange at a rate larger than or equal to 10-7 sec-1. The correlation time for enzyme-bound Mn2+-water interaction is frequency-dependent, indicating it to be dominated by the electron spin relaxation time of Mn2+. Formation of the ternary enzyme-Mn2+-mandelate complex decreases the number of fast exchanging water ligands by similar to 1, but does not affect tau-c, suggesting the displacement or occlusion of a water ligand. The competitive inhibitors D,L-alpha-phenylglycerate and salicylate produce little or no change in the enzyme-Mn2+-H2O interaction, but ternary complexes are detected indirectly by changes in the dissociation constant of the enzyme-Mn2+ complex and by mutual competition experiments. In all cases the dissociation constants of substrates and competitive inhibitors from ternary complexes determined by magnetic resonance titrations agree with K-M and K-i values determined kinetically and therefore reflect kinetically active complexes. From the paramagnetic effects of Mn2+ on 1/T1 and 1/T2 of the 13C-enriched carbons of 1-[13C]-D,L-mandelate and 2-[13C]-D,L-mandelate, Mn2+ to carboxylate carbon and Mn2+ to carbinol carbon distances of 2.93 plus or minus 0.04 and 2.71 plus or minus 0.04 A, respectively, were calculated, indicating bidentate chelation in the binary Mn2+-mandelate complex. In the active ternary complex of enzyme, Mn2+, and D,L-mandelate, these distances increase to 5.5 plus or minus 0.2 and 7.2 plus or minus 0.2 A, respectively, indicating the presence of at least 98.9% of a second sphere complex in which Mn2+, and C1 and C2 carbon atoms are in a linear array. The water relaxation data suggest that a water ligand is immobilized between the enzyme-bound Mn2+ and the carboxylate of the bound substrate. This intervening water ligand may polarize or protonate the carboxyl group. From 1/T2p the rate of

dissociation of the substrate from this ternary complex (larger than or equal to 5.6 times 10-4 sec-1) is at least 52 times greater than the maximal turnover number of the enzyme (1070 sec-1), indicating that the complex detected by nuclear magnetic resonance (NMR) is kinetically competent to participate in catalysis. Relationships among the microscopic rate constants are considered.

L7 ANSWER 89 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1975:27810 CAPLUS
DOCUMENT NUMBER: 82:27810
TITLE: Pyruvate carboxylase. Inhibition of the mammalian and avian liver enzymes by α-ketoglutarate and L-glutamate
AUTHOR(S): Scrutton, Michael C.; White, M. Dawn
CORPORATE SOURCE: Sch. Med., Temple Univ., Philadelphia, PA, USA
SOURCE: Journal of Biological Chemistry (1974), 249(17), 5405-15
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB α-Ketoglutarate was found to be a specific inhibitor of chicken liver pyruvate carboxylase. Addition of α-ketoglutarate caused the apparent KA for acetyl-Co A to become less favorable but did not affect the apparent Vmax. NMR, cold inactivation, and group-specific modification studies indicated that this kinetic interaction was noncompetitive. α-Ketoglutarate acted as a noncompetitive inhibitor when MgATP2- or pyruvate was the varied substrate. Secondary plots of slopes or intercepts were nonlinear functions of α-ketoglutarate concentration When HOC3- was the varied substrate, addition of α-ketoglutarate induced nonlinearity in the relation between reciprocal initial rate and reciprocal HCO3- concentration Further expts. suggested that the addition of this inhibitor caused the HCO3- sites in the enzyme to become kinetically nonidentical. In contrast, L-glutamate was approx. equally effective as a classical inhibitor of pyruvate carboxylase purified from chicken and rat liver. Inhibition of both enzymes was competitive with respect to MgATP2- and noncompetitive with respect to HCO3-. When acetyl-CoA was the variable component, addition of L-glutamate caused the apparent KA for the activator to become less favorable and also induced a small but significant decrease in the apparent Vmax. With pyruvate as the varied substrate, L-glutamate acted as a simple competitive inhibitor of chicken liver pyruvate carboxylase. Inhibition of the rat liver enzyme was a complex function of pyruvate concentration but approached competitive behavior at high concns. of this substrate. The apparent Ki for L-glutamate approximated 4mM for both chicken and rat liver pyruvate carboxylases. Interaction of α-ketoglutarate and L-glutamate at different sites on chicken liver pyruvate carboxylase was suggested both by the marked dissimilarities between the properties of inhibition by these 2 metabolites and by studies which demonstrated the absence of kinetic interaction between the 2 inhibitors. Apparently, chicken liver enzyme carries specific regulatory sites at which α-ketoglutarate interacts, while the inhibition patterns observed for L-glutamate appeared generally consistent with the proposal that this metabolite interacts at the α-keto acid site when the enzyme is in the form ,enzyme-biotin-CO2. Regulation of the catalytic activity of chicken liver pyruvate carboxylase by the α-ketoglutarate to L-glutamate ratio was also demonstrated under conditions which may approx. some parameters in the in vivo environment.

L7 ANSWER 90 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:79604 CAPLUS
DOCUMENT NUMBER: 80:79604
TITLE: Intrinsic catalytic activity of the zymogen, bovine

procarboxypeptidase A. Kinetic study using fluorine analogs
AUTHOR(S): Canonici, Patricia; Behnke, W. David
CORPORATE SOURCE: Dep. Chem., Univ. South Carolina, Columbia, SC, USA
SOURCE: Biochemical and Biophysical Research Communications (1974), 56(3), 575-9
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bovine Procarboxypeptidase A (I) has only until recently been considered catalytically inert. I, however, will hydrolyze the amide bond in simple acylated amino acids. Trifluoroacetyl-L-phenylalanine (II) is a very good substrate for the zymogen, exhibiting normal Michaelis-Menten kinetics with a Vmax near 2 + 103 min-1 and a Km of 2.6mM. Comparison of the pH-rate profiles for the zymogen-enzyme pair suggest that the same or similar groups are involved in the catalytic process in both proteins, further suggesting the preexistence of a considerable part of the enzyme active site in the zymogen. Moreover, trifluoroacetyl-D-phenylalanine is a competitive inhibitor of the hydrolysis of II and would appear a suitable analog to study enzyme (or zymogen)-inhibitor interactions by 19F-NMR during activation.

L7 ANSWER 91 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1973:487815 CAPLUS
DOCUMENT NUMBER: 79:87815
TITLE: Analogs of S-adenosylhomocysteine as potential inhibitors of biological transmethylation. Specificity of the S-adenosylhomocysteine binding site
AUTHOR(S): Coward, James K.; Slisz, Edwin P.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, USA
SOURCE: Journal of Medicinal Chemistry (1973), 16(5), 460-3
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of S-adenosylhomocysteine bearing alteration in the ribose moiety [e.g. cis-1'-(6-amino-9-purinyl)-3'-S-cyclopentylmethylhomocysteine (I) [2312-35-8]] were only weak inhibitors of purified rat liver catechol O-methyltransferase [9012-25-3], indicating the importance of these groups for binding of the cosubstrate, S-adenosylmethionine [29908-03-0], and the product, S-adenosylhomocysteine [979-92-0], to the enzyme. To synthesize II, 2-fluoroadenosine was converted to the 2',3'-isopropylidene derivative, then to the 5'-tosylate, treated with homocysteine [6027-13-0] in liquid NH3, and deblocked with N H2SO4, and the product was purified by chromatog. S-(2-fluoroadenosyl)homocysteine (II) [41935-07-3] was an effective competitive inhibitor at 1.3 mM and may be a useful 19F NMR probe of the active site of the enzyme.

L7 ANSWER 92 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1973:464378 CAPLUS
DOCUMENT NUMBER: 79:64378
TITLE: Early interactions between inhibitors and antibodies to lysozyme
AUTHOR(S): Rubio, Nazario; Portoles, Antonio
CORPORATE SOURCE: Inst. "Jaime Ferran" Microbiol., Cons. Super. Invest. Cient., Madrid, Spain
SOURCE: Immunochemistry (1973), 10(6), 361-4
CODEN: IMCHAZ; ISSN: 0019-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two lysozyme competitive inhibitors, histamine and D-acetyl-D-glucosamine, did not prevent precipitation of the enzyme by its antibodies, as it was demonstrated by immunol. techniques.

N-Acetyl-D-glucosamine prevented inhibiting antibodies from neutralizing lysozyme, as kinetic expts. and persistence of enzyme-inhibitor complexes detected by NMR spectroscopy revealed. This antibody fraction seemed to be nonpptg. The altered configuration of lysozyme in the enzyme-inhibitor complex might be the reason for this effect.

L7 ANSWER 93 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:129843 CAPLUS
DOCUMENT NUMBER: 80:129843
TITLE: Mechanism of the iron(II) activated enzyme, aconitase
AUTHOR(S): Villafranca, Joseph J.
CORPORATE SOURCE: Dep. Chem., Pennsylvania State Univ., University Park, PA, USA
SOURCE: Intra-Science Chemistry Reports (1972), 6(4), 73-83
CODEN: ISCRB6; ISSN: 0020-9848
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mitochondrial aconitase from pig heart is specifically activated by Fe(II), and both Mn(II) and Fe(II) compete for the metal site on aconitase. It is not known whether the metal ion is involved in a structural role or is at the catalytic center. Evidence is presented in support of a cyclic enzyme-metal-substrate bridge complex with the metal ion at the catalytic center. Catalytically inactive E-Mn(II)-S complexes were studied by the proton relaxation rate of water, using the 3 substrates of aconitase, citrate, isocitrate, and cis-aconitate. A ternary aconitase-Fe(II)-citrate complex was detected by continuous-wave NMR studies of the protons of citrate. This complex is a kineticaly competent species, since the 1st order rate constant for the breakdown of the ternary complex is greater than the maximum turnover number of the enzyme. All the NMR data indicate coordination of citrate by the enzyme-bound Fe(II). Enzyme-metal ion-inhibitor complexes were also studied, utilizing the inhibitors trans-aconitate, R(-)-citramalate and 1R:2R-fluorocitrate and models representing the competitive inhibition by these compounds are presented. Mechanisms for the stereospecific, irreversible inhibition by fluorocitrate are also presented.

L7 ANSWER 94 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:93478 CAPLUS
DOCUMENT NUMBER: 70:93478
TITLE: Aspartate transcarbamylase. A nuclear magnetic resonance study of the binding of inhibitors and substrates to the catalytic subunit
AUTHOR(S): Schmidt, Paul G.; Stark, George R.; Baldeschwieler, John D.
CORPORATE SOURCE: Stanford Univ., Stanford, CA, USA
SOURCE: Journal of Biological Chemistry (1969), 244(7), 1860-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binding of small mols. to macromols. can be studied by N.M.R. since the width of a resonance can often be related to rotational correlation times and exchange rates for bound and unbound species. Line widths for C-linked protons of analogs of carbamyl phosphate (carbamyl-P) in the presence of the catalytic subunit of aspartate transcarbamylase are a measure of the rotational freedom of the bound analogs. The protons of phosphonacetamide [(HO)2P(O)CH2CONH2] are broadened considerably in the presence of the subunit, while those of N-methylphosphonacetamide and methylphosphonate are not, indicating that an interaction between the NH2CO group of the analog and the enzyme limits rotation about the P-C bond in the 1st instance but not in the latter two. The resonance line width for the methylene protons of 0.025M succinate, a competitive

inhibitor of aspartate, is 0.48 Hz in the absence of enzyme at pH 7, increases slightly when catalytic subunit (20 mg. per ml.) is added, but increases to 2.00 Hz upon the further addition of 0.025M carbamyl-P. In this case, the broadening is due primarily to an increase in the lifetime of the succinate-enzyme complex, induced by carbamyl-P. Only analogs which are not larger than carbamyl-P and which have a carbonyl group in addition to a phosphate or phosphonate dianion induce the broadening of the succinate line. The resonance for the protons of malonate, another inhibitor of aspartate, is also broadened by carbamyl-P and phosphonacetamide in the presence of the catalytic subunit. Dissociation consts. determined at pH 7 confirm that carbamyl-P is the most effective analog in inducing succinate binding at this pH. In addition to line widths, chemical shifts of the bound species have been determined for some of the analogs. The chemical shifts suggest that an aromatic ring is near the binding site for phosphate.

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(FILE 'HOME' ENTERED AT 15:22:26 ON 04 DEC 2006)

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT 15:22:53 ON 04 DEC 2006

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L1          315 ENZYME (S) (COMPETITIVE OR ?COMPETITIVE) (S) INHIBI? AND NMR
L2            5 (LIBRARY OR SCREE? OR IDENTIF?) (S) (LIGAND OR COMPOUND) AND L1
L3            2 DUP REM L2 (3 DUPLICATES REMOVED)
L4        77053 (LIBRARY OR SCREE? OR IDENTIF?) (S) (LIGAND OR COMPOUND)
L5          101 PY>1999 AND L1
L6          214 L1 NOT L5
L7           94 DUP REM L6 (120 DUPLICATES REMOVED)
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=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	180.42	180.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.25	-11.25

FILE 'STNGUIDE' ENTERED AT 16:00:18 ON 04 DEC 2006

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 1, 2006 (20061201/UP).

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.82	186.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-11.25

STN INTERNATIONAL LOGOFF AT 16:58:35 ON 04 DEC 2006